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Air Pollution in High-Risk Sites–Risk Analysis and Health Impact

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1. Introduction

During the last century, at the top of industrialization phase, the excessive use of increasingly more complex inorganic and organic chemicals has caused serious environmental contamination all over the world with acute and chronic effects on population health.

The sites considered to be very contaminated and classified as dangerous are very numerous and often belong to industrial centres; in the past years, the contamination of soil and their contribution to air pollution have had an important role.

In countries characterized by a high socio-economic status, the industrial impact on air pollution is certainly less than the weight of traffic and urban heating, while in the developing and emerging countries, industrialization has still an important and unresolved role because of the lack of legislative management and control.

Epidemiological studies represent the scientific basis used to verify the existence of negative health effects caused by air pollution and to quantify the value of these effects, estimating the dose-response relationships. Many studies have demonstrated that air pollution is associated with a wide range of adverse health outcomes. Statistical analyses, conducted on monitoring and biomonitoring data, also show a relationship between the level of air pollution and the rate of mortality and morbidity. Unlike accidents, pollution is not considered a cause of immediate death. Actually, it is thought that it represents a cause of premature death. Air pollution is associated with a great number of illnesses, such as cancer, respiratory, cardiovascular and neurological diseases, and also diabetes and infertility problems.

The estimated cost of pollution becomes an economic evaluation of the risk of getting sick or dying prematurely. But the effects of pollution are particularly difficult to evaluate in terms

of quantity and cost. In order to assess the related risk of air pollution, it is certainly very important to establish the effects of pollution on human health, but it is also needful to consider some health determinants such as genetic factors, age, sex, and lifestyle habits.

Considering all these aspects, our proposal includes a chapter about atmospheric and urban pollution describing their relative and assessed effects on human health, with a detailed regard on risk assessment. In the last decades, a large number of legislations have been issued accepting international subscribed agreement, such as the Kyoto protocol, to save public health and restrict the effects of pollution on climate change. We will also focus on indoor pollution, with its insufficient data and relative problems and difficulties in management, on methodologies of study, and on some case reports.

2. Description of air pollution and characterization of monitored atmospheric pollutants

Air pollution, both for indoor or outdoor environments, is caused by several causes like chemical, physical, or biological modification of the natural characteristics of the atmosphere. Most common household combustion devices, motor vehicles, and industrial process are anthropogenic sources of air pollution, but also natural sources are very important for air pollution assessment as the forest fires and volcanoes emissions. Particulate matter, carbon monoxide, ozone, nitrogen dioxide, and sulphur dioxide today are the most important pollutants for their serious health risks [1].

In Europe, emissions of many air pollutants have decreased significantly the last 30 years, and air quality has improved across the region. However, excess of air quality standards still occurs, especially in metropolitan areas, and air pollutants released in one country may be transported in the atmosphere, polluting or degrading the air quality in neighbouring countries. On the basis of this statement, air pollution can be considered as a local, pan-European, and hemispheric issue [2].

At present, particulate matter, nitrogen dioxide, and ground-level ozone are recognized as the three most dangerous pollutants that affect human health, ranging in severity of impact according to long-term and peak exposures. Moreover, benzo(a)pyrene is a carcinogenic substance of increasing concern, as its concentrations are above the threshold set to protect human health in several urban areas, especially in central and eastern Europe. Air pollution could also represent a danger for the environment, producing acidification, eutrophication, and damage to agriculture.

There are various sources of air pollution, both anthropogenic and of natural origin, in turn divided in stationary and mobile sources. The most common anthropogenic sources of pollutants are combustion processes used for electricity generation, transport, industry and households, industrial processes and solvent use, agricultural crops and livestock, waste incinerator and landfill. A stationary source of air pollution, also known as a point source, refers to a fixed emission source, represented by factories, power plants, dry cleaners, resi-

dential wood burners, dry lakebeds, and landfills. A mobile source of air pollution is a source capable of moving under its own power. "On-road" transportation is related to all vehicles; however, there is also a "non-road" or "off-road" transportation, including the gas-powered machines for garden maintenance or recreational vehicles.

People or their activities do not cause natural "air pollution," and emission sources generally comprise volcanic eruptions, windblown dust, sea-salt spray, wild animals in their natural habitat, and plants releasing volatile organic compounds [2].

In the evaluation of pollution effects, it must be kept in mind that dangerous substances can be emitted as primary or secondary pollutants. Primary pollutants are emitted directly into the air from pollution sources, while secondary pollutants are formed when primary pollutants undergo chemical changes in the atmosphere. For example, NO_x and SO_2 are directly emitted into the air following fuel combustion or industrial processes. In contrast, O_3 and the major part of PM form in the atmosphere following emissions of various precursor species, and their concentrations depend strongly on meteorological conditions, such as high air temperatures and sunlight.

At present, the attention of scientist and legislator is focused on the major sources of dangerous substances, represented by urban and industrial activities.

In the evaluation of urban pollution, it is important to consider regional pollution, city pollution, real and *hot spot* events, determined by peaks of pollutants higher than average followed by gradual restoration of normal limits. Of these three components, the first two have direct effects on human and environmental health, as they expose population to contaminants for a longer time, causing chronic effects.

As regards industrial pollution, there are various unwanted substances and losses generated by industrial activities both for qualitative and quantitative aspects [3].

For this reason, to assess significant trends and to discern the effects of reduced anthropogenic precursor emissions, long time series of measurements and a continuous monitoring of air quality are needed [4].

The application of European Directives contained the emission of many pollutants, consequently reducing their levels in the atmosphere. However, while restrictions are imposed on industries, technologies are developed to reduce pollutants from road transport and the most harmful substances in the air are continuously monitored, air pollution is still a major problem and it is necessary to focus attention on its effects on human health and on methods to reduce these effects.

At present, based on "*The Clean Air Act*", Quality Standards are set for six common air pollutants, also known as "criteria pollutants". They are particulate matter, ground-level ozone, carbon monoxide, sulphur oxides, nitrogen oxides, and lead. These pollutants can harm human health and the environment and cause property damage. The set of limits based on human health is called primary standards. Another set of limits intended to prevent environmental and property damage is called secondary standards [5].

The main pollutants measured to characterize and monitor the quality of the environment are shown below.

2.1. Particulate Matter (PM)

PM is one of the most important pollutants in terms of potential to harm human health, as it penetrates into low regions of the respiratory system. PM is a complex heterogeneous mixture of solid particles and liquid droplets found in the air, whose size and chemical composition change in time and space, depending on different emission sources and atmospheric and weather conditions. These particles come in many sizes and shapes and can be made up of hundreds of different chemicals. PM includes both primary and secondary PM; primary PM is the fraction of PM that is emitted directly into the atmosphere from construction sites, unpaved roads, fields, smokestacks, or fires, whereas secondary PM forms in the atmosphere following the oxidation and transformation of precursor gases (mainly SO_2 , NO_x , NH_3) and some volatile organic compounds (VOCs) that are emitted from power plants, industries and automobiles.

Particle pollution includes "inhalable coarse particles," with diameters larger than $2.5\text{ }\mu\text{m}$ and smaller than $10\text{ }\mu\text{m}$, and "fine particles," with diameters that are $2.5\text{ }\mu\text{m}$ and smaller. Smaller sizes of PM such as $\text{PM}_{2.5}$, with a diameter up to $2.5\text{ }\mu\text{m}$, are considered particularly harmful due to their greater ability to penetrate deep into the lungs.

2.2. Tropospheric or ground-level ozone (O_3)

Ozone (O_3) is a secondary pollutant formed in the troposphere from complex photochemical reactions following emissions of precursor gases such as NO_x and non-methane volatile organic compounds (NMVOCs), deriving from paint application, road transport, dry-cleaning, and other solvent uses. At the continental scale, methane (CH_4) and carbon monoxide (CO) also play a role in O_3 formation. O_3 is a powerful and aggressive oxidizing agent, causing respiratory and cardiovascular problems and leading to premature mortality. High levels of O_3 can also damage plants, leading to reduced agricultural crop yields and decreased forest growth.

O_3 is found not only in the troposphere but also in the upper regions of the atmosphere. Three oxygen atoms constitute O_3 , and it is a very reactive molecule. O_3 in the upper atmosphere protects the earth from the sun's harmful rays, whereas the ground level O_3 is considered as the main component of harmful smog.

In fact, the tropospheric O_3 is created by chemical reactions between oxides of nitrogen (NO_x) and volatile organic compounds (VOC) after its emission in the air from industrial facilities and electric utilities, motor vehicle exhaust, gasoline vapours, and chemical solvents. O_3 is likely to reach unhealthy levels on hot, sunny days in urban environments and can also be transported through long distances by wind so that even rural areas can experience high O_3 levels.

O_3 contributes to what we typically experience as "smog" or haze, which still occurs most frequently in the summertime but can occur throughout the year in some southern and

mountain regions. Ground-level O_3 that we breathe can harm human health, especially affecting people with lung disease, children, older adults, and people who are active outdoors.

Children are at greatest risk from exposure to O_3 because their lungs are still developing and they are more likely to be active outdoors when O_3 levels are high, which increases their exposure. O_3 also damages vegetation, in particular, trees and plants during the growing season, and ecosystems, including forests, parks, wildlife refuges, and wilderness areas.

2.3. Carbon monoxide (CO)

Carbon monoxide (CO) is a very dangerous gas because it is odorless and it is emitted generally from all combustion processes both natural and anthropogenic sources. Urban air pollution is characterized by high CO emissions to ambient air from vehicles movement. CO can cause several harmful health effects, all related to reduced oxygen delivery to the body's organs (especially the heart and brain) and peripheral tissues causing death at very high doses of exposure.

2.4. Sulphur dioxide (SO_2)

Sulphur dioxide (SO_2) is emitted by the combustion of fuels containing sulphur. It contributes to acid deposition and can cause adverse effects on aquatic ecosystems in rivers and lakes, and damage to forests.

Sulphur dioxide (SO_2) is a highly reactive gas. SO_2 is emitted mainly by fossil fuel combustion by power plants (73%) and other industrial process (20%). Smaller sources of SO_2 are released by other industrial processes such as mineral extraction and also by the burning of high-sulphur fuels. Many illnesses are related to SO_2 ; particularly, harmful effects are linked to the respiratory system.

2.5. Nitrogen oxide (NO_x)

Nitrogen oxide (NO_x) is emitted during fuel combustion, by industrial facilities and the road transport. NO_x contributes to the formation of secondary inorganic PM and tropospheric O_3 , to acid deposition and to eutrophication. Of the chemical species that comprise NO_x , NO_2 is associated with adverse affects on health, such as inflammation of the airways and reduced lung function.

Nitrogen dioxide (NO_2) is a highly reactive gas. Other nitrogen oxides include the nitrous acid and nitric acid. EPA's National Ambient Air Quality Standard uses NO_2 as indicator for the class of nitrogen oxide. NO_2 is emitted from all vehicles and industrial plants, including power plants. In addition to the arising O_3 and PM, NO_2 is linked also to several adverse effects on the respiratory system. Both primary EPA standard (to protect health) and secondary EPA standard (to protect the public welfare) for NO_2 are established at 0.053 parts per million (53 ppb), averaged annually. EPA (January 2010) established an additional primary standard at 100 ppb. Primary standards are finalized to protect public health, including health of responsive populations, people with COPD, children, and the elderly. No European and extra-European countries have been found stranger to the problem.

2.6. Heavy metals

The main heavy metals in outdoor air are arsenic (As), cadmium (Cd), lead (Pb), mercury (Hg), and nickel (Ni); they are emitted mainly as a result of various combustion processes and industrial activities and generally can reside in or be attached to PM. Heavy metals are persistent in the environment and can be deposited on terrestrial or water surfaces, contaminating soils or sediments, and accumulating in food-chains.

2.7. Polycyclic Aromatic Hydrocarbons (PAHs) and benzo(a)pyrene (BaP)

PAHs are pollutants created during the incomplete burning of several organic substances like coal, oil, gas, wood, garbage, and also tobacco and smoked and grilled. Actually, there are more than 100 different PAHs identified. PAHs generally occur as complex mixtures of congeners. The primary sources of exposure to PAHs are inhalation of the compounds in tobacco smoke, wood smoke, and ambient air.

PAHs is a growing health concern in Europe, with particular regard to BaP, a polycyclic aromatic hydrocarbon, formed mainly from the incomplete burning of organic material such as wood and from car exhaust fumes especially from diesel vehicles. It is a known cancer-causing agent in humans. A main source of BaP in Europe is domestic home heating, in particular, wood burning, waste burning, coke and steel production, and mobile sources. Other sources include outdoor burning and rubber tyre wear. In Europe, BaP pollution is mainly a problem in certain areas such as western Poland, the Czech Republic, and Austria where domestic coal and wood burning is common.

Between the PAHs, the International Agency for Research on Cancer (IARC) considers BaP as 2A class, so carcinogen. However, the carcinogenicity of BaP was demonstrated through studies carried out with animals. Benzo(a)pyrene is a known mutagen, but it must be metabolized to be able to induce mutation. Exposure to BaP pollution is quite significant and ubiquitous. Central and Eastern European countries report air BaP concentrations above the target value. Approximately one quarter of the EU people were exposed to higher BaP concentrations respect to target value (1 ng/m^3) for the period 2008–2010. But almost the entire population was exposed to BaP concentrations above WHO reference level [6]. The increase of BaP emissions in Europe over the last years is therefore an important concern for public health. Regarding BaP, the Industrial Emissions Directive [7] regulates emissions from a large range of industrial sources.

2.8. BTEX

It is a group of chemical compounds including Benzene, Toluene, Ethylbenzene, and Xylenes. BTEXs are made up of naturally occurring chemicals that are found mainly in petroleum products such as gasoline. Everyone is exposed to small amounts of BTEX compounds in the outdoor air, at work, and in their homes. Besides the common daily exposures to BTEX, larger amounts can enter the environment from leaking underground storage tanks, overfills of storage tanks, fuel spills from auto accidents, and landfills.

Short-term exposure to gasoline and its components benzene, toluene, and xylenes has been associated with skin and sensory irritation, central nervous system (CNS) problems, and effects on the respiratory system. Chronic exposure to BTEX compounds can affect the kidney, liver, and blood systems. Long-term exposure to high levels of the benzene compound can lead to leukemia and cancers of the blood-forming organs [8].

2.9. Physical pollution

Physical pollution is pollution caused by colour (change), suspended solids, foaming, temperature conditions, or radioactivity, and it is characterized by its influence on environmental conditions caused by forces and operations of physics, such as noise, microwave radiation, vibration.

2.10. Microbiological factors

Microbiological factors in the environment represent an underestimated but insidious risk factor, which concern has increased with the introduction of advanced technologies in hospitals, industry, and agriculture. Microbial agents are transported and diffused in ambient through PM [9]. The main sources of microorganisms are Flüge droplets from human airways and conditioning systems, the last containing different bacteria such as *Legionella pneumophila*, virus, and mould.

To maintain a healthy environment, a strict monitoring must be undertaken for each of the contaminants mentioned above; legislation on environment sets a benchmark and provides a series of actions to hold the values of the contaminants within the limits.

As air pollutants can be transported many miles away from the area of their emission, monitoring these substances is more difficult than monitoring contaminants in water or soil, so it was decided to record ambient air quality data focusing on major pollutants. Continuously operating automatic analysers are the most important information source on air pollution levels [10]. According to current legislation, measurements are taken at permanent sites equipped with physico-chemical monitoring devices even if these stations provide only data on exposure levels which do not facilitate making conclusions on the effects or impacts to human health and the general environment. Moreover, spatial coverage and temporal definition of the carried measurements together with meteorological conditions influence the degree of representativeness of the data compared to the real state of pollution of the study area [11].

Recently, innovative technologies have been developed and direct damage of harmful effects can be demonstrated by monitoring living organisms, called biomonitors, which provide a measure of integrated exposure over a certain amount of time taking into account also climatic conditions and enrich the substance to be determined so that the analytical accessibility is improved and the measurement uncertainty reduced. Moreover, sampling is relatively simple and no expensive technical equipment is needed. The field of biomonitoring includes bioindication of effects and bioaccumulation of pollutants [12].

The information provided by mosses, lichens, and higher plants on the deposition on the effects of air pollutants is an important complement to the data acquired with automatic systems. Distribution of tree species on a national or supranational lets you draw cheaply and in a short time maps of diffusion and deposition of persistent pollutants or the effects of tropospheric O₃ and other phytotoxic pollutants [13].

3. Statistical methodologies to evaluate the risk assessment and air pollution correlated diseases

Extreme pollution episodes that took place in the period 1930–1960 have initiated the epidemiological studies for increase of health environmental concern. The association between air pollution and certain health variables was made clear by several studies [14, 15].

Thanks to the new approach, air pollution levels were reduced substantially, such that, for health effects assessment, now, longer monitoring plans are required. To this end, epidemiologists began to use some statistical models. In the 1970s firstly were used the dynamic regression models, models in which the relationship between the dependent and explanatory variables were distributed over time rather than being expected to occur simultaneously. However, the problem of these types of models is that they assume that the dependent variable is distributed normally, but this is a condition extremely rare to achieve [16].

In the 1990s were used for the first time the linear models based on Poisson regression because the event counts more typically have a Poisson distribution. These models use the “time” and its transforms as variable [16].

Also Poisson regression is particularly useful only when cases rather than the entire population can be enumerated.

Nevertheless, Poisson regression poses the problem that, if any of these unmeasured variables follows a cyclical component of varying frequency, the parametric functions of time cannot be easily adapted. So, these limitations led to the development also of nonparametric Poisson regression [17], which is well adapted to the irregular cyclic components of unmeasured variables reducing any potential confounding.

One difficulty with this method is that the researcher must specify the number of degrees of freedom, with several discrepancies arising as the way to calculate this. Because inappropriate determination of the number of degrees of freedom is frequently a bias in the estimates of nonparametric Poisson designs, epidemiologists focused on the case-crossover (CCO) [18] design that purported to control time trends. The CCO design is characterized by the fact that each subject serves as his or her own control. This design was initially used to assess the effect of exposures measured at an individual level and was not applicable to exposures with a time trend, such as air pollution. A variant was developed to bypass this bias [19], the bidirectional CCO, characterized by having control time periods before and after the event. This design was already appropriate for ecologic-type exposures, such as air pollution, water pollution, etc. In addition, pollution values are not affected by the presence of prior morbidity and mortality

events. In fact, in the CCO design in air pollution, pre- and post-event exposure values are independent of the hazard-period exposure; those that are post-event referent can be appropriate. One advantage of CCO design respect to Poisson regression is its ability to assess potential effect modification at the individual level rather than at the group level [20]. As an alternative analytic methodology to Poisson regression, the CCO approach allows for direct modeling of interaction terms, rather than depending on multiple subgroup analyses [20].

Besides the individual characteristics during the statistical analysis of epidemiological data, other variables must be considered, taking into account that the chemical characteristics of air pollutants mixture and PM may change over time and depending on the geographical location, emission sources, atmospheric chemistry, and weather conditions [21].

Interest in health effects of air pollution became more intense after two US cohort studies suggested that exposure to fine PM in the air was associated with life shortening [22,23].

Exposure to pollutants such as airborne PM and O₃ has been associated with increases in mortality and hospital admissions mainly because of respiratory and cardiovascular disease, due to both acute and chronic exposure [24].

Health problems can include cancer, respiratory irritation, nervous system problems, and birth defects.

Air pollution, in the year 2012, was responsible for 3.7 million deaths, i.e., approximately 6.7% of the total deaths. In particular, air pollution is estimated to cause deaths from lung cancer (16%), COPD (11%), ischemic heart disease and stroke (>20%), and respiratory infection (13%). Furthermore, the IARC announced that it has classified outdoor air pollution as carcinogenic to humans (Group 1).

Typically, exposure to toxic components of air pollutant causes the well-established correlated diseases, respiratory and pulmonary ones, such as decreased lung function and increased incidence of chronic cough, bronchitis, chronic obstructive pulmonary disease, asthma, and conjunctivitis [25,26,27].

Recent clinical and epidemiological data suggest also that cardiovascular disease may be related to pollution [28,29] especially those associates with fine PM [30,31,32,33]. The PM's effects on the cardiovascular system seem to involve the activation of prothrombotic factors, leading to thrombosis, but destabilization of atherosclerotic plaques cannot also be excluded. In addition, there may be direct effects on the heart or indirectly on the nervous system.

Health effects have been seen at very low levels of exposure, and it is unclear whether a threshold concentration exists for PM and O₃ below which no effects on health are likely.

It could be expected that the impact caused by a preventable risk factor would decline if the exposure to that risk factor could be reduced or removed. According to this approach, the proportional reduction in the number of health problems or deaths as a result of reducing the risk factor is known as the attributable fraction (AF) [34].

Public health agencies concerned with air quality perform risk assessments to determine the increased risk of illness from a specific human exposure to a toxic air pollutant.

The risk assessment approach outlined by the WHO in the Environmental Burden of Disease (EBD) series [35,36] includes the following steps:

1. assessment of the air exposure of the population through data from Air model or monitoring networks. A target concentration is also needed to determine the attributable disease or the potential gains of a management plan;
2. sufficient number of persons exposed to air pollutants;
3. baseline data of incidence of the adverse health outcomes associated with air pollutants (like mortality rate); and
4. concentration-response functions (CRFs) related to the incidence of adverse health effects.

The US Environmental Protection Agency (US-EPA) divided the risk assessment process into the following four steps:

- a. **Hazard Identification:** it allows determining the potential human health effects from exposure to a chemical. This is based on information provided by the scientific literature.
- b. **Dose-Response Assessment:** it is the assessment of the relationship between a dose of chemical exposure and incidence or severity of the related adverse health effect. It takes into consideration the intensity and pattern of exposure and also age and lifestyle variables that may affect people's susceptibility. The dose-response relationship is evaluated differently for carcinogenic and non-carcinogenic pollutants. In fact, for carcinogens, it is assumed that there is a linear relationship between an increased dose of exposure and increase in cancer risk; this is expressed as slope factor (SF) and threshold is not accepted. For risks evaluation by inhalation of carcinogenic substances, US-EPA use the potency slopes to develop the unit risk factors (URFs). A URF is the upper-bound excess probability of contracting cancer as the result of a lifetime of exposure to a carcinogen at a concentration of $1 \mu\text{g}/\text{m}^3$ in air. For inhalation effects from non-carcinogens, dose-response data are used to develop reference concentrations (RfCs) for both long-term and short-term exposures. Unlike carcinogens, non-carcinogens are assumed to have thresholds dose, so the injury does not occur until exposure has exceeded a threshold limit. An RfC is derived from a no-observed adverse effect level (NOAEL) or lowest observed adverse effect level (LOAEL) determined through human or animal exposure studies.
- c. **Exposure Assessment:** it determines the extent (intensity, frequency, and duration, or dose) of human exposure to a chemical in the environment.
- d. There are three components to exposure assessment:
 - i. Estimation of the maximum quantity of each pollutant emitted from the source.
 - ii. For each contaminant emitted, estimation of the resulting maximum annual average and (where applicable) maximum short-term average ambient air concentrations, using dispersion models, or air impact values based on dispersion models.
 - iii. Estimation of the amount of contaminant taken in by a human receptor.

e. **Risk Characterization:** it is the final step in risk assessment where health risk is calculated and described thanks to data collected in the first three steps.

- **Carcinogens**

Human health risk estimates for inhalation of carcinogenic air pollutants are based on the following:

$$\text{Cancer Risk} = C \times \text{URF}$$

where

C = maximum annual average ambient air concentration of a pollutant ($\mu\text{g}/\text{m}^3$)

URF = pollutant-specific inhalation unit risk factor ($\mu\text{g}/\text{m}^3$)⁻¹

For routes of exposure other than inhalation, risk is calculated by multiplying the estimated chemical dose (in mg/kg/day) by the chemical-specific oral slope factor (in (mg/kg/day)⁻¹).

- **No carcinogens**

Human health risk estimates for inhalation of non-carcinogenic air pollutants are based on the following:

$$\text{Hazard Quotient} = C/\text{RfC}$$

where

C = maximum ambient air concentration, $\mu\text{g}/\text{m}^3$

RfC = pollutant-specific reference concentration, $\mu\text{g}/\text{m}^3$

The averaging time can be either annual, or a specific number of hours, depending on the basis of the reference dose [37]. For routes of exposure other than inhalation, the hazard quotient is calculated by ratio between the estimated chemical dose (in mg/kg/day) and the chemical-specific reference dose (in mg/kg/day).

Hazard quotients can be summed (separately for inhalation and oral exposures and for different averaging times) to give a hazard index.

4. Evaluation of indoor air pollution and comparison with the urban and high-risk sites

Clean air is a fundamental health determinant. The quality of indoor air (e.g., homes, offices, schools, day care centres, public buildings, where people spend a large part of their life). Hazardous substances emitted from buildings, construction materials, and indoor equipment

or due to all human activities indoors lead to a broad range of health problems and may even be fatal for infants and children. Indoor environmental issues are still an open topic of public health, including health risks and the means by which human exposures can be reduced [38].

Mistakes of evaluation or unacknowledged by public about health risks associated with a variety of indoor environmental pollutants and sources of pollution (e.g., radon, mold and moisture, secondhand smoke, and indoor wood smoke) cause a minor efficacy of prevention and/or risk's low perception. In poorly ventilated dwellings, smoke in and around the house can exceed acceptable levels for fine particles 100-fold [39] with respect to outdoor levels already known. In fact, inadequate ventilation can increase indoor pollutant levels for incomplete dilution of these. High temperature and humidity levels can also increase concentrations of certain pollutants [40]. Outdoor air enters and leaves a house by infiltration, natural ventilation, and mechanical ventilation. If infiltration, natural ventilation, or mechanical ventilation is poor, the air exchange rate is low and pollutant levels can increase rapidly [41].

There are several sources of indoor air pollution including combustion of oil, gas, kerosene, coal, wood, and tobacco products; building materials and furnishings as diverse as deteriorated, asbestos-containing insulation, wet or damp carpet, cabinetry and objects made with certain pressed wood products (e.g., formaldehyde, pesticides, etc.); products for household cleaning and their maintenance (phtalates, bisphenol A, fragrances, pesticides, detergents, chlorine bleach, lye, ammonia, etc.), cosmetics for personal care (solvents, phtalates, bisphenol A, fragrances, mineral oil, ethoxylated surfactants and 1,4-dioxane, formaldehyde, lead, oxybenzone, parabens, toluene, triclosan, etc.), chemicals used for hobbies (solvents, lead, pesticides, mineral oil, cadmium, manganese dioxide, cobalt, formaldehyde, aromatic and chlorinated hydrocarbons, ethylene glycol monomethyl ether, ethylene glycol monobutyl ether, etc); central heating and cooling systems and humidification devices (mold, viruses, fungi, bacteria, mycotoxins, etc.); and outdoor sources such as radon, pesticides, and outdoor air pollution likely to come into the house where can concentrate. Some of these sources (building materials, outdoor sources, wood furnishings, etc.) release pollutants more or less continuously. Other sources, related to activities carried out in the home, release pollutants intermittently, and their concentrations can remain in the domestic air for long periods after these activities. The relative importance of any single source depends on how much of a given pollutant it emits and by the proven hazard of those emissions. In some cases, factors such as how old the source is and whether it is properly maintained are very significant (e.g., an improperly functioning gas stove can emit more CO than one that is properly adjusted).

Exposure to indoor air pollution is particularly high among women and young children who spend the most time in the domestic environment, and health effects may be shown soon after exposure or years later.

According to WHO, 4.3 million people a year die from the exposure to household air pollution [39]. In fact, especially cooking and heating with solid fuels (wood, charcoal, etc.) produce high levels of smoke both in and around the home and this contains a large variety of health-damaging pollutants [42].

Immediate effects such as irritation of the eyes, nose, and throat; headaches; dizziness; and fatigue may show up after a single acute exposure or repeated sub acute exposures. These are usually treatable and have short-term effects. Oftentimes, the simple elimination of a person's exposure to the identified source of pollution is sufficient for restoring health.

An additional problem is the recurrent multiple indoor pollution exposure of residents, complicating and amplifying the health effects [43].

Exposure to indoor air pollution leads to a wide range of respiratory diseases [39, 44] such as lung cancer [45, 46], ischemic heart disease [46], stroke [46], and cataract [46].

There is emerging evidence, although based on fewer studies, that suggests that household air pollution, especially in developing countries, may also increase the risk of other important child and adult illnesses such as the following:

- low birth weight and perinatal mortality (still births and deaths in the first week of life) [45, 46],
- asthma [39, 45],
- otitis media (middle ear infection) and other acute upper respiratory infections [39],
- tuberculosis [45],
- nasopharyngeal cancer [39],
- laryngeal cancer [39], and
- cervical cancer [39].

Also exposure to unhealthy concentrations of fine PM has been connected to increased respiratory/cardiovascular illnesses [39, 47]. In fact, the smaller air particles can penetrate into the deeper lung. PM is being linked to adverse birth outcomes [46], neurodevelopment, cognitive function [48], and diabetes [39].

Semple et al. [49] said that median $PM_{2.5}$ concentrations from 93 smoking homes were $31 \mu\text{g}/\text{m}^3$ (ranged between 10 and $111 \mu\text{g}/\text{m}^3$) and $3 \mu\text{g}/\text{m}^3$ (ranged between 2 and $6.5 \mu\text{g}/\text{m}^3$) for the 17 non-smoking homes and still showed that non-smokers living with smokers typically have average $PM_{2.5}$ exposure levels more than three times higher than the WHO guidance for annual exposure to $PM_{2.5}$ ($10 \mu\text{g}/\text{m}^3$). So, $PM_{2.5}$ pollution in indoor ambient where smokers live is approximately 10 times higher than that of non-smoking. A non-smoker living with a smoker is exposed to same $PM_{2.5}$ of a non-smoker living in a heavily polluted city such as Beijing. This condition is likely to be greatest and dangerous for the very young and for older members of the population because they typically spend more time at home. Zhou and colleagues [50] have demonstrated that in New York City, despite the ban on tobacco smoking, some hookah bars still serve tobacco-based hookahs, and in these particular indoor environments, the authors have found elevated concentrations of pollutants that may present a real health threat to visitors and employees. The mean real-time $PM_{2.5}$ level was $1179.9 \mu\text{g}/\text{m}^3$, whereas the filter-based total PM mean was $691.3 \mu\text{g}/\text{m}^3$. The mean real-time black carbon level was $4.1 \mu\text{g}/\text{m}^3$,

organic carbon was $237.9 \mu\text{g}/\text{m}^3$, and CO was 32 ppm. Airborne nicotine was present in all studied hookah bars ($4.2 \mu\text{g}/\text{m}^3$).

Dorizas et al. [51] with their study showed that in nine naturally ventilated primary schools of Athens (Greece) during spring, PM concentrations were significantly affected by the ventilation rates and presence of students. Both PM_{10} and $\text{PM}_{2.5}$ were greater during teaching than the non-teaching hours, and, in many cases, the $\text{PM}_{2.5}$ concentrations exceeded their limit values. For most of the cases, the indoor to outdoor concentrations ratios of PM_{10} and $\text{PM}_{2.5}$ were much greater than one, indicating that the indoor environment was being mostly affected by indoor sources instead of the outdoor air. Furthermore, it was found that chalk and marker board usage significantly affects indoor pollutant concentrations.

No similar characteristics were found between indoor pollution and urban and high-risk sites outdoor pollution, because the poor ventilation of houses and buildings in general allows the concentration of chemical and biological pollutants that are not found in similar outdoor concentrations also in severe pollution event. Urban outdoor air pollution refers to the air pollution which the populations are exposed to, living in and around the urban area. Indoor air pollution refers to the pollutants found in indoors. An important difference is in the heavy metals concentration, generally most abundant and with major variability of species in urban and industrial air outdoor pollution compared with indoor pollution.

At the moment, in Italy, a reference rule has not been set. For this reason, until today, the main information concerning some guidelines or reference values in indoor air is obtained by the international scientific literature or by the few guidelines issued by other European countries or, for analogy, by other guidelines values regarding outdoor air. However, public health awareness on indoor air quality still lags significantly behind that of outdoor air quality.

The main areas at high risk of environmental crisis in Italy are described below.

5. Case reports: ILVA-Taranto, Melilli-Priolo-Augusta sites, Gela and Milazzo emerging situation, "Terra dei Fuochi" and Seveso

In order to cope with the huge problem of pollution, experts were mobilized at national and regional levels in the drafting of numerous scientific papers in order to initiate actions to protect health in the areas most affected by the emission of high quantities of contaminants. In many cases, the results of these studies support arguments about correlation between the exposition to pollutants and outbreak of neoplastic diseases; however, for some areas, it has been highlighted that there is a higher incidence in urban areas rather than in sites of national interest, leading to speculation about the etiologic implication of non-industrial contaminants.

At the moment in Italy, the industrial pole of Taranto, Melilli-Priolo-Augusta, Gela e Milazzo sites, and "Terra dei fuochi" and the outcome of the tragedy that occurred in 1976 in Seveso represent the most interesting areas for their extension and extent of involved population. An overview of current developments of studies and the status of remediation undertaken in these areas will be given below.

5.1. ILVA-Taranto

Founded in 1961, ILVA of Taranto is a steel plant at full cycle, where occur all the steps that lead from iron ore to steel [52–54]. The plant, which is partially impounded by order of the judiciary, is the largest steel maker in Europe. The area of Taranto is identified at high risk of environmental crisis because of an extensive industrial area developed close to the urban settlement. Industrial activities are responsible for environmental pollution, mostly due to polycyclic aromatic hydrocarbons (PAHs), heavy metals, organic solvents, polychlorinated biphenyls (PCBs), PM, and dioxin.

Table 1 shows the main pollutants found in soil, ground waters, and sediments of the area of Taranto.

Soil	antimony, arsenic, beryllium, cadmium, cobalt, chromium total, chromium VI, mercury, lead, nickel, zinc, copper, vanadium, cyanide, hydrocarbons C <12 and C"/> 12, PAHs, benzene, xylene, dioxins
Subsurface	antimony, arsenic, beryllium, cadmium, cobalt, chromium total, chromium VI, mercury, lead, nickel, zinc, copper, vanadium, cyanide, hydrocarbons C <12 and C"/> 12, PAHs, benzene, xylene, dioxins
Groundwater	arsenic, selenium, aluminium, iron, manganese, nickel, lead, cobalt, total chromium, chromium VI, cyanides, sulphates, nitrates, BTEXS, PAHs, hydrocarbons and MTBE
Sediments	arsenic, nickel, lead, total chromium, copper, mercury, zinc, total PAHs, PCBs

Table 1. Main pollutants found in soil, ground waters, and sediments of the area of Taranto

To define the extent of the health risk, rigorous epidemiological studies have been conducted to assess both the short-term effects that occur in acute as a result of rapid changes in the concentrations of pollutants and the long-term effects caused by prolonged exposures and which occur 10–15 years after the start of exposure.

In 2006, the Ministry of Health has funded a project called “SENTIERI” (Studio Epidemiologico Nazionale dei Territori e degli Insediamenti Esposti a Rischio da Inquinamento - National Epidemiologic Study of the Territories and Settlements Exposed to Risk from Pollution) with the purpose to analyse the mortality of populations residing in proximity of a number of industrial agglomerates which by their nature potentially have a high factor of hazardous health and/or environmental contamination such as to be classified as SIN (Sites of National Interest for the Remediation).

The population of Taranto has been the subject of several multi-centre epidemiological studies that have documented the role of air pollution on the increase in short-term and long-term effects [52,53].

Epidemiological analysis of the residents of the city revealed death rates from all causes, for lung, pleura, and bladder cancer and for non-Hodgkin lymphoma. A case-control study on

incident cases of these diseases in Taranto suggested a possible link between risks and residence close to the sources of emissions.

A recent study called EpiAir in which subjects were recruited rigorously and it was taken into account the exact georeferencing of areas of residence and employment analysed the spatial variability of air pollutants in Taranto and showed that atmospheric pollution in this city is not distributed homogeneously, but it is mainly widespread in the areas adjacent to industrial pole. In the results of this study have been taken into account the socio-economic status and calculated indices of deprivation; these aspects have a great importance, as many individual habits, such as cigarette smoking, alcohol consumption, physical activity, and obesity, are often associated with social status so that the adjustment made for the socio-economic factor has also adjusted the individual variables not directly measured, providing very reliable data. Moreover, in this study, mortality rate and hospitalization rate were measured to evaluate both long- and short-term effects. Data about mortality are reliable, as 98% of the causes of death were recovered, thanks to the linkage of personal data with the database of the ASL and show an excess of mortality for cancer, cardiovascular, and respiratory diseases. As far as hospital admissions, evaluated from hospital discharge schedule, were concerned, it was difficult to get accurate data because the comparison was made only on the hospital area of Taranto, without taking into account the extra-regional mobility and the secondary diagnosis. Although these are limited, data show an increase of hospitalization for the abovementioned causes. The results of this study have strengthened the argument that there is a correlation between exposure to emissions from the steel plant of Taranto and an increase of cancer and cardiovascular and respiratory diseases [55].

The European Environment Agency, in the list that shows the 622 most polluting industrial plants in Europe, included more than 60 Italian companies; Ilva of Taranto is placed second. As a result, the situation with the city of Taranto and Ilva is currently the subject of discussion and great concern [53,54,56]. To control the situation in the area were enacted several regional laws aiming to carry out the assessment of environmental impact and damage health in order to take targeted action to protect the environment and public health. Moreover, in the Italian Act 6 of February 2014, strategies are defined to make the remediation of contaminated areas from emissions of ILVA.

5.2. Sicily air quality

In Sicily, four Sites of National Interest have been individuated and the industrial areas of Melilli-Priolo-Augusta (Siracusa), Gela (Caltanissetta), and Milazzo (Messina) have been declared by national and regional legislation "areas high risk of environmental crisis." It is likely that the excesses of mortality and morbidity observed in areas of Melilli-Priolo-Augusta, Gela, and Milazzo are attributable to occupational exposures and environmental concerns related to the number of plants and the consequent contamination of environmental matrices [57], although the last reports show how these rates do not exhibit a significant increase.

5.2.1. Melilli-Priolo-Augusta sites

The large industrialized coastal area of eastern Sicily within the territory of the municipalities of Augusta, Priolo Gargallo, and Melilli is defined "petrochemical pole of Siracusa." These

territories started to be subject to industrialization in 1948 with the construction of a refinery (the RA.SI.O.M), and in the following years, other industrial facilities were born; currently, the petrochemical pole hosts five refineries of petroleum products, two centrals of ENEL, a gas plant and cogeneration, a factory of magnesite, a cement plant, a purifier of industrial and urban waste and a shipyard.

In these areas, the increase in the number of illness might be linked with PM, which are released into the atmosphere from industrial chimneys and have the ability to convey inside the body, through the lung, every kind of pollutants from the atmosphere. The residents, who have expressed their concerns to environment organizations and public health institutions, have also noted this potential association.

Official data on emissions point out a long list of definitely carcinogenic and teratogenic chemicals (acrylonitrile, benzene, cadmium, hexavalent chromium, nickel, silicon, vanadium, dioxins, and furans), and many other potential hazards, according to the IARC (Agency International Agency for Research on Cancer).

About PM, the main substances contained in it are represented by heavy metals as shown by the results of a study conducted by the Faculty of Agriculture of the University of Palermo, which used lichen for biomonitoring as their action of bio-accumulators for heavy metals, highlighting a significant presence of these hazardous metals in the environment concerned [57, 58].

These pieces of evidence induced the Ministry of the Environment to recognize the Priolo-Augusta-Melilli site as "an area in environmental crisis for which it has become necessary a legislative and Financial able to address in a timely manner the dramatic emergency." The large amount of epidemiologic studies conducted in these areas highlights the role of atmospheric pollution in the development of some cancers although recent data published by AIRTUM (Associazione Italiana dei Registri Tumori – Italian Association of cancer registries) [59] show that the higher incidence of cancer in Sicily is found in the city of Catania and in other metropolitan areas, such as Palermo and Messina, as well as in big countries like Acireale and Gravina, leading to hypothesize the role of other risk factors probably linked to road traffic and unhealthy lifestyle, contributing in the outbreak of above mentioned diseases. According to the last published report, the industrial sites are not among the areas with the highest incidence of cancer, as supposed, and surprisingly, the SIN of San Filippo del Mela does not present excess in the incidence of tumors.

5.2.2. Gela and Milazzo emerging situation

In the area of Gela and the surrounding area rises one of the main industrial centres of the island. The area, declared "area at high risk of environmental crisis," includes the municipalities of Gela, Niscemi, and Butera. Within the bounded area subjected to remediation, there is a large industrial centre, consisting of plants for refining and extraction of crude oil and petrochemical plants. In particular, productions include polyethylene, molten sulphur, sulphuric acid and phosphoric acid, ammonia and fertilizer complexes [57].

The environmental impact of the refinery of Gela comes mainly from emissions into the atmosphere and the consequent presence of pollutants such as SO_2 , NO_x , dust, H_2S , and CO . Conveyed emissions are mainly generated in the combustion process and are coming out of the chimneys.

Data provided by ARPA (Regional Agency for Environmental Protection) reveal exceedances in ambient town, some parameters such as benzene, methane, hydrocarbons, and PM_{10} containing heavy metals such as nickel. A scientific study has shown that the entire area of Gela is heavily influenced by emissions of metals and non-metals from both car traffic or vehicular pollution and industrial pollution. In particular, the study highlights pollution of the particulate present in the aerosol analysing the deposition of the particulates on pine needles. The analysis of pine needles is a fast method for monitoring the pollutants present in the air: the pine needles provide information for the long-term impact of even low levels of pollutants. As for neoplastic diseases, it has not been shown that there is an excess of incidence in this area, although some Sicilian studies highlight an increase of Relative Risk for these diseases compared to other areas of the Region not characterized by the presence of industrial agglomerates. Moreover, in this area, an important role is played by the current wind, responsible for the transport of substances emitted by plants in Gela for long distances, interestingly in particular to Niscemi where contamination of soils by the above mentioned pollutants was found.

The industrial area of Milazzo is characterized by the presence of a large industrial centre, including an oil refinery, a thermoelectric central, a co-generator, a steel mill, a plant for the recovery of lead from spent batteries, and different other smaller factories. In the vicinity of industrial installations, there are several common installations, among which are those belonging to "area at high risk of crisis environment."

A single study carried out in Milazzo area reveals that children are exposed to elevated concentrations of sulphur dioxide, nitric oxide, and $\text{PM}_{2.5}$. In more weeks, the average concentration evaluated for sulphur dioxide has exceeded $20 \mu\text{g}/\text{m}^3$, and the $\text{PM}_{2.5}$ average in the study period was about $23 \mu\text{g}/\text{m}^3$, i.e., twice the WHO air guideline limit. Also, epigenetic markers were associated with air pollutant concentrations – particularly with regard to the nitric oxide pathway [57, 58].

5.3. Terra dei fuochi

One of the greatest environmental and health criticality that covered Italy in the last two decades is linked to the illegal waste disposal, triggering serious repercussions both in the territories concerned and the health of the residents in these areas and leading the Institutions to take actions that stiffen confidence in themselves and protect the health of the population. Studies carried out in the areas affected by this phenomenon, although not definitive, confirmed an increase in health risks resulting from waste disposal, highlighting in particular an increase in mortality from all causes, the excesses of mortality from specific cancers (liver, lung, stomach, kidney, and bladder) as well as an increase in non-neoplastic diseases of the respiratory system. The limits of ecological studies mainly reside in the fact that it is not possible to assess the individual characteristics of involved subjects, data on the amount and types of

substance emitted are not exact, and therefore, extent of population exposure is not certain and estimates arising from these studies do not provide reliable data on the correlation. Despite the necessity of deepening the studies above, on February 2014, the Italian Parliament approved a law for the protection of these specific areas, which has as main innovations the request for a mapping of polluted areas and crops of these territories, the allocation of funds to carry out a health screening, and the introduction of the crime of burning waste.

This law, if one side has paid attention on the problem, on the other hand has created problems for the application of screening, excellent in itself as a means of prevention, but totally inappropriate to the case in question. It should be noted that on such land occurred the burning of hazardous waste, even radioactive in nature, and that substances emanating from these processes have not been proven to be in correlation with cancers for which screening is scheduled (colorectal, breast, cervix). Moreover, alarmism generated by media has also created skepticism in consumers, even internationally, with a substantial drop in sales of the excellent products from Campania.

However, contrasting the illegality and protecting public health is a duty of the institutions, as well as civic, and to implement the cited actions, the Institutions with the collaboration of experts gathered in the Technical Committee for the Contaminated Territories (CTTC) that provide information on correct methodology to implement the definition of the criteria for the mapping of sites, for the identification of specific diseases to perform a targeted screening, and for implementing the operations of monitoring and remediation.

5.4. Seveso

On July 1976 in Meda (Italy) at the chemical plant ICMESA (Industrie Chimiche Meda Società Azionaria) occurred the Seveso disaster [60]. During the usual production of trichlorophenol, a fungicide, an uncontrolled reaction that sparked the safety valves of the tank reactor took place, releasing the deadly chemical vapour into the atmosphere. About 3000 kg of toxic cloud compound containing dioxin TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) was released into the air. The wind immediately dispersed the toxic cloud eastwards: the dioxin could begin to generate its catastrophic effects, affecting the inhabitants of the area and also making uninhabitable the territory on which it was deposited.

The chemicals released into the air from the ICMESA were carried by the wind and caused the contamination of, mainly, four municipalities: Seveso, Meda, Desio, and Cesano Maderno.

Since no one was at the plant when it happened, the seriousness of the disaster was not immediately observed.

Dioxin has been considered to be the most toxic human-made substance; the Seveso disaster represents the highest known TCDD exposure to residential populations and probably the most studied dioxin contamination incident in history [60, 61].

The most common sign of human health problems was skin disorder. The immediate effects on the population were evident especially from a dermatological point of view: after two days

already appeared the first cases of chloracne, a disease that is documented to be associated with dioxin.

In order to estimate health problems of population, a great number of laboratory tests were carried out on blood samples. In 1987, it became possible to measure low levels of dioxin in blood samples. Another important effect of the dioxin exposure concerned reproduction, in particular affecting the sex ratio (a higher proportion of females were born in the first 7 years after the accident). In addition, a large number of pregnancies ended as spontaneous abortions were reported.

The affected places still show signs of contamination. The new EU legislation on industrial equipment of chemical and their coordinated management was started in June of 1982, when the Council of Ministers approved the European Union's Council Directive 82/501/EEC, the Seveso Directive.

A central part of the directive was made by reference to the obligation of transparent public information about industrial accidents, as well as new security measures to be taken in case of an accident [60, 61].

The new concept was approved for industrial workers and the public, the right to know the substance and the form of the problems that could threaten them and the exact operation of the safety procedures.

6. Conclusions

From the analysis of situation in the sites at risk of environmental crisis on the Italian territory, the greatest criticalities are represented by the effects of emissions from industrial plants although increasing attention must be paid to the effects of vehicular traffic, as shown by recent data of RTI report, according to which the highest incidence of neoplastic diseases is recorded in areas characterized by the presence of large urban agglomerations.

As regards the comparison between the role of indoor and outdoor pollution in the onset of diseases related to environmental exposure, the second is still predominant and, in the case of sites of national interest, indoor air pollution can be regarded as a factor that may enhance the effects induced by outdoor pollutants.

Pollution situation is controlled through the application of numerous laws on environmental protection, which in our country are very stringent and thanks to which it was possible at least to contain both the emission of pollutants and their effects on human health.

The effect of environmental stressors on human health and policy-making today can be explained using the Driving Force-Pressure-State-Exposure-Effect-Action (DPSEEA) model [62]. Ideal environmental management is based on a reduction of environmental risk exposure, as well as the risks themselves, in all stages of the process. However, this policy-based intervention is not accurate or simple for several motifs (problematic approach for many variables as time lag between exposure reduction to environmental stressor and its negative

effects on health or, e.g., as many other variables) that make the intervention very difficult to implement [63]. For DPSSEA model application, the national policy-based intervention, finalized to air pollutants reduction, is very closely to the air quality standards, as the setting-up of those standards can lead to management and reduction of sources of pollution so decreasing pollutant concentrations and subsequent relevant health risk factors to ensure healthy residents [62, 64]. Moreover, air quality standards setting may be considered to be a reliable method for reducing exposure to air pollutants.

Although Institutions have implemented several containment measures, environmental pollution neither has nor ceased to be a problem of Public Health. Currently, in Italy, there are about 15,000 sites to characterize, reclaim, and monitor that represent more than 2% of the entire territory and require the allocation of 25–30 billion euros.

To solve this problem, firstly, rigorous epidemiologic studies must be previewed and conducted, taking into account a careful evaluation phase to confirm the association between environmental exposure and health effects. Epidemiological studies should provide for a careful characterization of the sites, taking into consideration that the great variety of production processes gives rise to an equally wide variety of pollutants not known and for which are not yet known metabolism and mechanisms of interaction with other substances present or released into the environment.

Performing a thorough epidemiological investigation is essential to proceed to risk assessment and risk management. In the management of this route, greater emphasis must be attributed to activities of prevention departments and ARPA and technical committees consisting of experts who can give useful indications to legislators to improve and promulgate laws to protect collective health and must perform a central role. The aim of this cooperation is achieving a “sustainable risk,” that is, the risk that remains after the interventions of control and prevention and that can be more easily managed by the competent bodies.

Nonetheless, it is necessary to consider that the bases to make the most of these actions are the training of the operators and the information, so that in this view, activities of continuous updating for public health professionals are promoted.

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